REMARKS

Applicants thank the Examiner for reconsidering and withdrawing the § 103 (obviousness) rejection over Ohuchida et al. (U.S. Patent 7,176, 240) and Sramek et al. (Opin. Invest. Drugs, 2002).

Amendment of Claims

Applicants have amended claim 44, the sole independent claim, to recite "A method for treating cognitive impairment associated with Mild Cognitive Impairment. . ." This amendment is supported in the specification as filed at, e.g., page 11, lines 9-16 and page 83, lines 1-5.

The above amendment contains no new matter.

Applicants request entry of the claim amendment.

THE NEW REJECTION

Rejection under 35 U.S.C. § 103

Claims 44 and 53 stand newly rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Haas et al., Annals of Clinical Psychiatry, 1997, 9(3), 145-147 ("Haas") in view of Petersen et al., Neurology 2001, 56, 1133-1142 ("Petersen").

According to the Examiner, Haas refers to a treatment for demented, elderly, aggressive patients with divalproex, a 1:1 mixture of sodium valproate and valproic acid, and recites that divalproex had utility in the "treatment of behavioral dys[c]ontrol in cognitively impaired individuals." The Examiner concedes that Haas fails to teach treating Mild Cognitive Impairment (MCI). The Examiner, however, asserts that Petersen recites that dementia is often preceded by MCI, and that MCI refers to the clinical state of an individual who has impaired memory but otherwise functions well and

does not meet the clinical criteria for dementia. The Examiner then contends that it would have been obvious to one of ordinary skill in the art at the time the invention claimed in this application was made to combine Haas and Petersen "with a reasonable expectation for success in arriving at a method of treating MCI by administering a composition comprising valproate." In particular, the Examiner argues that because "it was known that valproate treated the symptom of full-blown cognitive impairment seen in dementia, one would expect that, because dementia follows MCI, and would be expected to have the same etiology, valproate would be expected to exert some therapeutic benefit (e.g., improvement of cognitive function) on a subject with MCI, as observed for the subject with full-blown cognitive impairment." The Examiner further asserts that if a compound is known to treat a certain medical condition, that compound would then be expected to treat the conditions leading up to said condition. Applicants traverse.

In his newly-minted rejection, the Examiner is following the same faulty logic that doomed the previous Ohuchida/Sramek rejection. In that rejection, the Examiner argued that because (1) MCI precedes AD and (2) some MCI patients develop AD, potential treatments for AD would be obvious to use in the treatment of MCI. Here, the Examiner is arguing that because (1) MCI precedes dementia and (2) some MCI patients develop dementia, potential treatments for dementia would be obvious to use in the treatment of cognitive impairment in MCI.

As before, when the actual facts are considered, the rejection falls like a house of cards.

First and foremost, contrary to the Examiner's statement in paragraph 12 of the Office Action, Haas does not report treating the "symptoms of full-blown cognitive impairment seen in dementia." Haas reports only that divalproex improved behavioral dyscontrol in cognitively impaired older people. *See* page 146, right column, 2nd paragraph. Haas did not report that divalproex had any effect on cognitive impairment in dementia, much less in MCI. Indeed, Haas said exactly the opposite (page 147, left column, paragraph 1):

> Although there are no studies to show that divalproex is useful in reversing the cognitive impairment of brain damage, our experience and that of others indicate it to be highly effective at decreasing unmanageable and/or dangerous conduct in elderly demented patients.

By contrast, cognitive impairment, not behavioral dyscontrol, is the hallmark of MCI. In fact, the Examiner cites with approval Petersen's statement that MCI refers to the clinical state of an individual who has impaired memory but otherwise functions well, i.e., there is no behavioral dyscontrol. *See* Office Action, paragraph 10. Thus, the skilled worker would have no reasonable expectation that divalproex would treat MCI given (1) that Haas reports only that it treats a symptom of dementia – behavioral dyscontrol – that is not present in MCI patients and (2) that Haas reports that divalproex does not treat cognitive impairment – the *sine qua non* of MCI and its treatment. On that basis alone, applicants request that the Examiner reconsider and withdraw the rejection.

In order to reflect the importance of treating cognitive impairment in the context of treating MCI as disclosed in this application, applicants have amended claim 44, the sole independent claim, to recite " A method for treating cognitive impairment associated with Mild Cognitive Impairment. . ."

Secondly, Petersen does nothing to cure the defects of Haas in the context of treating MCI and its hallmark cognitive impairment. Petersen reports that, while MCI sometimes precedes dementia (MCI patients have "increased risk for developing dementia" (Petersen, Abstract)), MCI is clinically distinct from dementia. Thus, Haas' treatment of dementia says nothing about the treatment of the clinically distinct MCI. Even if Petersen, however, had established an etiological relationship between dementia and MCI (which it does not), the combination of Haas and Petersen would still fail to render the claimed invention obvious. Haas only refers to divalproex treating behavioral dyscontrol, not cognitive impairment. Petersen does not remedy that gap. Petersen provides no connection between behavioral dyscontrol and cognitive impairment. Therefore, one of skill in the art would have no reasonable expectation that a treatment for behavioral dyscontrol in dementia would also treat cognitive impairment in MCI.

In fact, Haas makes crystal clear that the behavioral dyscontrol and cognitive impairment are completely unrelated. As applicants have demonstrated above, Haas acknowledges that "there are no studies to show that divalproex is useful in reversing the cognitive impairments of brain damage (page 147, left column, paragraph 1)". Thus, Haas, even if combined with Petersen's "increased risk" report, *teaches away* from the claimed invention. A skilled practitioner at the filing date, considering Haas, even in view of Petersen, would not even attempt to treat MCI and the cognitive impairment that is its hallmark with valproate and certainly would have no reasonable expectation that such treatment would be successful.

For at least the above reasons, the claimed invention is not obvious over Haas and Petersen, individually or in combination.

Applicants request that the Examiner reconsider and withdraw the obviousness rejection and allow the two amended claims.

CONCLUSION

Applicants request favorable consideration of and early allowance of amended claims 44 and 53. The Examiner is invited to telephone the undersigned to discuss any issue pertaining to this response or the pending claims.

Respectfully submitted,

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